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The development of the tocoflexols, a series of novelvitamin E analogues with enhanced bioavailability

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Vitamin E is composed of two series of closely related compounds, tocopherols and tocotrienols; which show a widely varying degree of biological effectiveness. In recent years, the tocotrienols have gained considerable attention because of their beneficial effects in areas such as radiation protection, cholesterol reduction and cancer treatment and prevention. Unfortunately, the potential of the tocotrienols has been hampered because their very short circulation half-life severely limits their bioavailability.

Using state-of-the-art computational techniques, we have developed the tocoflexols, which are designed to overcome the limitations of the tocotrienols. This was achieved by a novel approach in which we created analogues that more effectively use the natural mechanism of retention of vitamin E components in the body. Specifically this was accomplished by designing compounds that are better accepted by alpha-tocopherol transfer protein, the liver enzyme that controls the circulation levels of vitamin E. By maintaining the bioactivity of the tocotrienols while achieving enhanced bioavailability, these compounds may have a strong potential as therapeutic agents.

Structural modification of drugs to take advantage of endogenous transport systems is a novel and intriguing concept whose potential is just starting to emerge. Successful demonstration of its usefulness in this application is likely to encourage development of similar strategies for the future drug design and development in other areas of biomedical sciences.

Biography

Cesar M. Compadre has extensive research experience, on the development of bioactive compounds based on naturally occurring compounds, and on the use of molecular modeling in drug design and structure-activity studies. He has published over papers and over 70 patents related to the development of bioactive compounds, and one FDA approved antimicrobial technology. He has a B.S Pharm degree, and obtained his Ph.D. degree in Medicinal Chemistry and Pharmacognosy, from the University of Illinois at Chicago. He conducted postdoctoral research on structure-activity relationships studies using molecular modeling at the University of Illinois and at Pomona College working with Professor Corwin Hansch. Additionally, he had a sabbatical experience at NASA Ames Research Center in computer modeling. At the University of Arkansas for Medical Sciences he established and directs the molecular modeling facility. He has extensive research collaborations with many scientists locally, nationally and internationally.

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